Indian Journal of Clinical Biochemistry, 2003, 18 (1) 46-51

TISSUE POLYPEPTIDE SPECIFIC ANTIGEN IN THE POST THERAPEUTIC EVALUATION OF PATIENTS WITH OVARIAN AND COLORECTAL CANCER

Sharmila Upadhya* , Subramanya Upadhya and D.M. Vasudevan*****

**Department of Biochemistry, Kasturba Medical College, Manipal*
***Department of Physiology, Kasturba Medical College, Manipal*
****Department of Biochemistry, Manipal Institute of Medical Sciences, Sikkim*

SHORT TITLE: TPS in Ovarian and Colorectal Cancer

ABSTRACT

The study was designed to evaluate the significance of tissue polypeptide specific antigen (TPS) in patients with histologically proven ovarian and colorectal cancer following treatment along with CA125 (in ovarian cancer) and CEA (in colorectal cancer). Patients were grouped as follows :

Group I: Patients with stable disease

Group II: Patients with metastasis and relapse

In patients with ovarian and colorectal cancer, the mean TPS levels were significantly higher in patients of group II compared to group I. The percentage of patients above cut-off levels for TPS were 17.4% in group I and 95.5% in group II. Similar results were observed with the mean levels of CA125. In colorectal cancer patients, the percentage of patients above cut-off levels for CEA and TPS were 70% and 30% in group I and 100% in group II for both the markers. Our observations indicate that TPS may be used as a common marker to indicate metastases in patients with ovarian and colorectal cancer.

KEY WORDS

TPS, CA125, CEA, Ovarian cancer, Colorectal cancer

INTRODUCTION

Tissue polypeptide specific antigen (TPS) is a differentiation and proliferation marker that is elevated in a variety of cancers like head and neck cancer (1), gynecological cancer (2,3), prostatic cancer (4,5), gastrointestinal cancer (6) and breast cancer (7). Recently the trend in the use of tumor markers is to use multiple markers to increase the sensitivity of detection of metastases. Usefulness of a single marker to indicate metastases in various malignant conditions is a matter of debate. The present study was conducted to evaluate the usefulness of TPS along with the conventional markers in ovarian cancer and colorectal cancer after therapy.

Author for correspondence:

Sharmila Upadhya
Department of Biochemistry,
Kasturba Medical College, Manipal-576 119
E-mail: shardhya@yahoo.com
Telephone: 571201 Ext. 22326
Fax: 70062

MATERIALS AND METHODS

45 patients with histologically proven ovarian cancer and 20 patients with histologically proven colorectal cancer were chosen for the study. All patients had undergone ablative surgery along with two courses of chemotherapy postoperatively. Based on the clinical response, patients were grouped as:

Group I: Included patients who had responded to therapy. They were in clinical remission with no clinical evidence of metastasis (Stable disease)

Group II: Included patients who had not responded to therapy; there was clinical evidence of local or distant metastasis (Progressive disease).

Of the 45 patients with ovarian cancer, 23 patients were in group I and 22 patients were in group II and of the 20 patients with colorectal cancer, 10 patients

were in each group. Serum samples were obtained from these patients during the follow up period i.e., 4-6 months following treatment. Levels of CA125 in patients with ovarian cancer and CEA in patients with colorectal cancer were estimated by the IM_x immunoassay system. TPS was estimated in all patients using the kit from Beki Diagnostics, Bromma, Sweden.

Statistical analyses were done between the groups in ovarian cancer and colorectal cancer by the nonparametric Mann Whitney U test, using Statview version 3 software package. Correlation was analyzed between CA125 and TPS in ovarian cancer and CEA and TPS in colorectal cancer. Correlation was confirmed by the Fisher's r to z test.

RESULTS

The CA125 (in U/ml) and TPS levels (in U/L) (mean±SEM) in patients with ovarian cancer are 17.9±2.9 and 47.9±8.5 in patients with no clinical evidence of metastasis (groupI). The CA125 and TPS levels in group II patients (mean ±SEM) are 219±47.4 and 283±37. Mean CA125 and TPS levels in group II were significantly increased compared to group I (P=<0.0001, P=<0.0001). There was a significant correlation between CA125 and TPS levels (n=45, r=0.411, P=0.004). The cut-off levels used for CA125 was 35U/ml (8) and for TPS was 85U/L (9) respectively. Cutoff levels for CA125 were 95th percentile of the serum CA125 concentration in healthy controls (8). In the study, TPS levels were estimated in 100 healthy subjects. The cutoff values of 85 U/L for TPS was determined on the basis of ROC curve analysis (9). The percentage of patients above cut-off levels in group I were 8.7% (2 out of 23 patients) and 17.4% (4 out of 23 patients) for CA125 and TPS. In group II, the percentage of patients above cut-off levels was 95.5% for both the markers.

CEA levels in ng/ml are 11.8+1.7 and 102+14 (mean±SEM) in group I and group II patients with colorectal cancer. The TPS levels in U/L (mean +SEM) were 73.4+13.7 and 243.3+36.5 in group I and group II patients respectively. Mean CEA and TPS levels are significantly higher in group II compared to group I (P=0.0002, P=0.0004). There was a significant correlation between CEA and TPS levels (n=20, r=0.667, P=0.0009). The percentage of patients above cut-off levels for CEA (10ng/ml) (10) were 70% (7 out of 10 patients) and 100% (10 out of 10 patients) in group I and II. And, the percentage of patients above cut-off levels for TPS (85 U/L) were 30% (3 out of 10 patients) and 100% (10 out of 10 patients) in groups I and II. The levels of TPS in groups I and II in ovarian and colorectal cancer are compared in figures 1 and 2.

DISCUSSION

Tissue polypeptide specific antigen (TPS) assay detects the M3 epitope of cytokeratin 18 or of tissue polypeptide antigen. Cytokeratin 18 is an acid type cytosolic protein expressed in simple epithelial cells and also by tumor cells (11). TPS is a good proliferative marker and indicates tumour cell proliferative activity. TPS was found to be more sensitive than CEA, CA19-9 and CA125 in advanced gastrointestinal cancer. Also, TPS correlated best with the course of the disease (6) and with the outcome of treatment in advanced gastrointestinal cancer (12). TPS levels were good predictors of survival in Duke's stage D of colorectal cancer (13). In our study, we have found that CEA and TPS are elevated above cut-off levels in all patients with metastatic colorectal cancer. Also, the levels of CEA and TPS were higher in patients with progressive disease compared to patients with no evidence of disease progression. Similar to our results, Mishaeli *et al* have reported that TPS levels were elevated in patients with metastases compared to patients with no evidence of disease after therapy in colorectal cancer (14). Griesenberg *et al* have reported that a combination of clinical investigation, imaging methods and determination of tumor markers in diagnosis and follow up of colorectal cancer in preoperative and postoperative phases increases the chances of diagnosis of recurrent colorectal cancer (15). TPS was also more sensitive than CEA in detecting relapse (12).

TPS and CA125 levels were higher in patients with metastatic (progressive) ovarian cancer compared to patients with stable disease, following therapy, in our study. High levels of TPS and CA125 were also reported in ovarian cancer compared to benign gynecological diseases. TPS and CA125 were higher in advanced stages of cancer compared to early stages (2,16). It was observed that serum TPS and CA125 reflect the course of the neoplastic process during chemotherapy (17). Also, TPS and CA125 levels could be used as good predictors of recurrence in ovarian cancer (16). TPS in combination with CA125 has improved the detection of recurrent ovarian cancer (8) and in combination they increase the prognostic accuracy after chemotherapy (18).

A significant correlation was observed between CA 125 and TPS levels and overall survival in patients with FIGO stages III and IV after three courses of chemotherapy in patients with ovarian cancer. The prognostic value of these markers was higher when both CA 125 and TPS levels were measured (19). The combined use of CA125 and TPS during chemotherapy had a better negative predictive value than when the markers were used alone (20).

In our study, we have observed that TPS is elevated in 95.5% of patients with metastatic ovarian cancer and 100% of patients with metastatic colorectal cancer. This indicates that TPS is a good indicator (marker) of metastases in ovarian and colorectal cancer. However, it may not be able to replace CA125 in the diagnosis of ovarian cancer (17). TPS may be used as a prognostic tool to assess the severity of disease during follow up. Whereas the markers like CEA and CA125 are relatively specific for a given malignancy, markers like TPS can be used as a common indicator of metastases in a variety of malignancies.

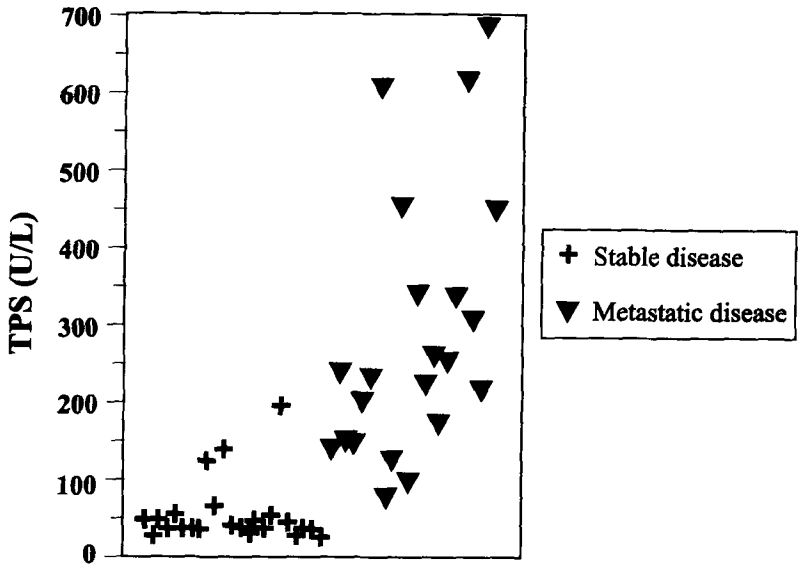

Fig. 1 : TPS levels in U/L in patients with ovarian cancer in patients with stable disease and with metastatic disease

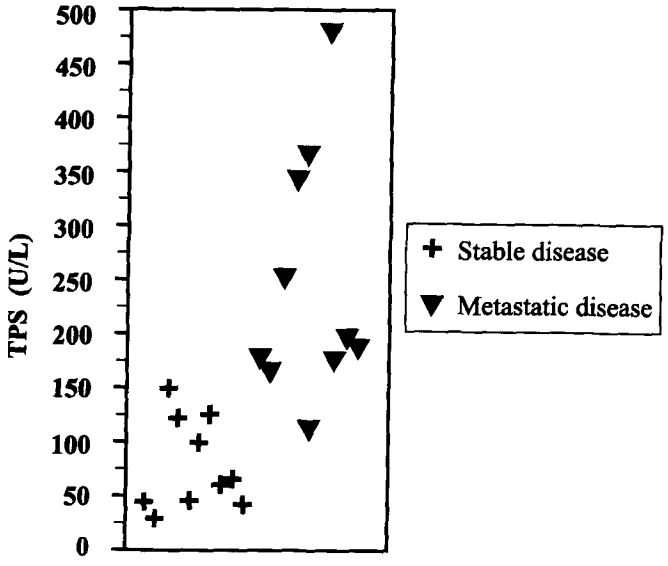

Fig. 2 : TPS levels in U/L in patients with colorectal cancer

REFERENCES

1. Molina, R., Torres, M.D., Moragas, M., Filella, X., Jo, J., Gimenez, N., Traserra, J. and Ballesta AM. (1995) Prognostic value of TPS in patients with head and neck malignancies: comparison with SCC. Anticancer Res. 15, 479-84

2. Sarandakov, A., Phocas, I., Botsis, D., Sikiotis, K., Rizos, D., Kalambokis, D., Trakakis, E. and Chryssikopoulos, A. (1998) Tumour-associated antigens CEA, CA125, SCC and TPS in gynaecological cancer. Eur J. Gynaecol. Oncol. 19, 73-7

3. Tempfer, C., Hefler, L., Haeusler, G., Reinthaller, A., Koebl, H., Zeisler, H. and Kainz, C. (1998) Tissue polypeptide specific antigen in the follow up of ovarian cancer and cervical cancer patients. Int. J. Cancer 79, 241-4

4. Kramer, G., Steiner, G.E., Madersbacher, S., Stulnig, T., Lang, T. and Marberger, M. (1997) Serial tissue polypeptide specific antigen determination in the follow up of hormone treated carcinoma of prostate. J. Urol. 158, 1446-51

5. Theyer, G., Holub, S., Durer, A., Andert, S., Haberl, I., Theyer, U. and Hamilton, G. (1997) Measurements of tissue polypeptide antigen and prostate specific antigen in prostate cancer patients under intermittent androgen suppression therapy. Br. J. Cancer 75,1515-8

6. Kornek, G., Schenk, T., Raderer, M., Djavarnmad, M. and Scheithauer, W. (1995) Tissue polypeptide antigen in monitoring palliative treatment response of patients with gastrointestinal tumours. Br. J. Cancer 71, 182-5

7. Locker, G.J., Mader, R.M., Braun, J., Seider, A.E., Marosi, C., Rainer, H., Jakesz, R. and Steger GG. (1995) New mucin-like cancer-associated antigens (CA M26, CA M29, CA549) and a new proliferation marker (TPS) in patients with primary or advanced breast cancer. Oncology 52, 140-4

8. Sluitz, G., Tempfer, C., Kainz, C., Mustafa, G., Gitsch, G., Koelbl, H. and Biegelbayer, C. (1995) Tissue polypeptide antigen and cancer associated serum antigen in the follow up of ovarian cancer. Anticancer Res 15, 1127-9

9. Ceraini, L., Giovanella, L., Salvadore, M., Bono, A.V. and Roncari, G. (1997) TPS immunoassay in the diagnosis and clinical staging of prostatic carcinoma. Comparison with PSA. Int. J. Biol. Markers 12, 27-34

10. Hanke, B., Reidel, C., Lampert, S., Happich, K., Martus, P., Parsch, H., Himmler, B., Hohenberger, W., Hahn, E.G. and Wein, A. (2001) CEA and CA19-9 measurement as a monitoring parameter in metastatic colorectal cancer under palliative first line chemotherapy with weekly 24 hr infusion of high dose 5-fluorouracil and folinic acid. Ann. Oncol. 12, 221-6

11. Bodenmuller, H. (1995) The biochemistry of CYFRA 21-1 and other cytokeratin tests. Scand. J. Clin. Lab. Invest. Suppl. 221, 60-6

12. Glimelius, B., Hoffman, K., Einarrson, R., Pahlman, L. and Graf, W. (1996) Monitoring palliative chemotherapy in advanced gastrointestinal cancer using serial tissue polypeptide antigen. Acta Oncol. 35, 141-8

13. Carpelan-Holmstorm, M., Haglund, C., Lundin, J., Alfthan, H., Stenman, U.H. and Roberts, P.J. (1996) Independent prognostic value of preoperative serum markers CA 242, specific tissue polypeptide antigen and human chorionic gonadotrophin beta, but not of carcino embryonic antigen or tissue polypeptide antigen in colorectal cancer. Br J. Cancer 74, 925-9

14. Mishaeli, M., Klein, B., Sadikov, E., Bayer, I., Koren, R., Gal, R., Rakowsky, E., Levin, I., Kfir, B., Schachter, J. and Klein, T. (1998) Initial TPS serum level as an indicator of relapse and survival in colorectal cancer. Anticancer Res. 18, 2101-5

15. Griesenberg, D., Nurnberg, R., Bahlo, M. and Klapdor, R. (1999) CEA, TPS, CA 19-9 and CA 72-4 and fecal occult blood test in the preoperative diagnosis and follow-up after resective surgery of colorectal cancer. Anticancer Res. 19, 2443-50

16. Shabana, A. and Onsrud, M. (1994) Tissue

polypeptide specific antigen and CA125 as tumour markers in ovarian carcinoma. Tumour Biol. 15, 361-7

17. Zygmunt, A., Madry, R., Markowska, J. and Fischer Z (1999). Estimation of the usefulness of neoplastic markers TPS and CA125 in diagnosis and monitoring of treatment in ovarian cancer. Eur. J. Gynaecol. Oncol. 20, 298-301

18. Van Dalen, A., Favier, J., Burges, A., Hasholzner, U., de Bruijn, H.W., Dobler-Girdziunaite, D., Dombi, V.H., Fink, D., Giai, M., McGing, P., Harlozinska, A., Kainz, C., Markowska, J., Molina, R., Sturgeon, C., Bowman, A. and Einarrson, R. (2000) Prognostic significance of CA 125 and TPS levels after 3 chemotherapy courses in ovarian cancer patients. Gynaecol. Oncol. 79, 444-50

19. Van Dalen, A., Favier, J., Baumgarter, L., Hasholzner, U., De Bruijn, H., Dobbler, D., Dombi, V.H., Fink, D., Giai, M., McGing, P., Harlozinska, A., Kainz, C., Markowska, J., Molina, R., Sturgeon, C., Bowman, A. and Einarrson R (2000). Serum levels of CA 125 and TPS during treatment of ovarian cancer. Anticancer Res. 20, 5107-8

20. Senapad, S., Neungton, S., Thirapakawong, C., Suphanit, I., Hangsubcharoen, M. and Thaminton K (2000). Predictive value of combined serum CA125 and TPS during chemotherapy and before second-look laparotomy in epithelial ovarian cancer. Anticancer Res. 20, 1297-300